Reviewer's report

Title: Psychiatric disorder in early adulthood and risk of premature mortality in the 1946 British Birth Cohort

Version: 1 Date: 29 December 2010

Reviewer: Hiram Wildgust

Reviewer's report:

1) Major Compulsory Revisions

The cohort selected is well documented and is an excellent source of data for this study. The data analyses all appear to be valid and correct.

However, I do have a concern about the mortality pattern found in this study, which appears to be very atypical with a very high cancer death rate compared with CVD deaths (I obtained data from their earlier publication (reference 25) which showed that cancer mortality is roughly 90% higher than CVD mortality in this cohort). Below, I have listed studies showing % CVD and cancer deaths in SMI patients and the general population which show very different mortality patterns to this study (CVD => cancer deaths in the below studies).

Since no data is available either in this paper or earlier publications to examine externally whether the cancer rates in this study are high, low or normal compared with the general population, this makes it difficult to understand what is happening in terms of mortality in this cohort.

Therefore, the compulsory revision which I ask, is that the authors calculate standardised mortality rates SMRs (all cause, cancer and CVD) so that the mortality data in this cohort has some external reference, or the authors address this issue in another way to give it external validity. In the SMI studies below, SMR rates are calculated for each study.

Literature review mortality in SMI patients and the general population showing %CVD and %cancer mortality

Capasso et al (Schizophrenia research (2008) 98: 287-289) reported a study with 55 years follow up, finding 29% CVD deaths and 19% cancer deaths. Chong et al (J Clin Psychopharmacology (2009) 29: 5-8) reports a rate of 17% for both CVD and cancer deaths. The most recent UK prospective data (Brown et al, (2010) 196: 116-121) reported 15% deaths due to CVD and 8% cancer deaths with a mean age very similar to the data in this paper with a mean follow up of 25 years. Flegal et al (2008) reported on the mortality pattern for 2004 in the USA which showed that deaths comprised of 37% CVD and 24% cancer (Flegal, JAMA. 2007; 298(17):2028-2037)

2) Minor Essential Revisions
3) Discretionary Revisions

a) limitations

It would be helpful if the authors could comment on the findings in the literature that incidence rates for disorders (CVD, cancer etc) in SMI patients do not always explain mortality rates. Some examples from the literature are shown below.

Literature findings

Lawrence et al (Act Scan (2000) 101:382-388), Kisely (Canadian J Psychiatry (2008) 53:753-761) & (Canadian J Psych (2009) 176:779-784), Laursen (Arch General Medicine (2009) 66:713-720), Mitchell (British J Psychiatry (2009) 194:491-499) report excess cardiac or cancer mortality in SMI patients which are not fully explained by incidence rates. The above authors propose a number of explanations which include either issues of health screening, starting treatment later or poorer access to and or poorer quality of health care. It would be helpful for the authors of this paper to include comment on this important point.

b) Are the discussion and conclusions well balanced and adequately supported by the data?

Could the authors comment on a recently published study (Kilbourne et al. Gen Hospital Psychiatry (2009) 31:555-563) which showed that for major depression or bipolar disorder that the associated heart disease mortality risk was similar to patients without these diagnoses. This study was a very large cohort (>10,000), followed up for over 8 years and controlled for both behavioural and clinical risk factors and the findings are very different from the finding by the current authors that psychiatric disorders had a 84% higher mortality risk than those with no disorder.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

My only financial interests are consultancy and lecture fees from Eli Lilly & Company Ltd